Attorney Docket No. 09095.0009 Application No.: 09/888,840

$$R^1$$
 R^2
 R^3

or a pharmaceutically acceptable salt or prodrug thereof, wherein at least one of R¹or R³ is a pyrimidine;

R², R⁴ and R⁵ are each independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, cyano, nitro, cycloalkyl, carboxaldehyde, and a group of formula II defined as

subject to the proviso that one or more than one of R¹ or R³ is a group of formula II as defined above;

wherein D, B, Y and Z at each occurrence are independently selected from the group consisting of -CR⁶=, -CR⁷R⁸-, -C(O)-, -O-, -SO₂-, -S-, -N=, and -NR⁹-;

n is an integer of zero to three;

R⁶, R⁷, R⁸ and R⁹, at each occurrence, are each independently selected from the group consisting of hydrogen, alkyl, carboxy, hydroxyalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl and carboxyalkyl; and

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R¹⁰ and R¹¹ are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxyalkyl, alkoxycarbonylalkyl, carboxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl and heterocyclylamino; or

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R¹⁰ and R¹¹ are taken together with N to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring, substituted with one or more than one substituent R¹³, wherein R¹³, at each occurrence is independently selected from the group consisting of alkyl, alkylene, alkoxy, alkoxyalkyl, cycloalkyl, aryl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclylalkylaminocarbonyl, hydroxy, hydroxyalkyl, hydroxyalkoxyalkyl, carboxy, carboxyalkyl, carboxycarbonyl, carboxaldehyde, alkoxycarbonyl, arylalkoxycarbonyl, aminoalkyl, aminoalkanoyl, aminocarbonyl, carboxamido, alkoxycarbonylalkyl, carboxamidoalkyl, cyano, tetrazolyl, alkanoyl, hydroxyalkanoyl, alkanoyloxy, alkanoylamino, alkanoyloxyalkyl, alkanoylaminoalkyl, sulfonate, alkylsulfonyl, alkylsulfonylaminocarbonyl,

wherein A is an unsubstituted aryl group, an unsubstituted heterocyclyl group, a substituted aryl group, or a substituted heterocyclyl group, substituted with

arylsulfonylaminocarbonyl and heterocyclylsulfonylaminocarbonyl;

one or more than one substituent R¹², wherein R¹², at each occurrence, is

independently selected from the group consisting of halogen, alkyl, aryl,

haloalkyl, hydroxy, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxyalkoxy,

hydroxyalkyl, aminoalkyl, aminocarbonyl, alkyl(alkoxycarbonylalkyl)

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4.) C

aminoalkyl, heterocyclyl, heterocyclylalkyl, carboxaldehyde, carboxaldehyde hydrazone, carboxamido, alkoxycarbonylalkyl, carboxy, carboxyalkyl, carboxyalkoxy, hydroxyalkylaminocarbonyl, cyano, amino, heterocyclylalkylamino, carboxythioalkoxy, carboxycycloalkoxy, thioalkoxy, carboxyalkylamino, trans-cinnamyl and heterocyclylalkylaminocarbonyl; and

- wherein R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹² and R¹³ are unsubstituted or substituted with one or more than one electron donating or electron withdrawing group
- wherein the heterocyclyl is chosen from 4-, 5-, 6- and 7-membered rings containing 1-3 heteroatoms independently selected from nitrogen, oxygen and sulfur; the 4- and 5-membered rings have zero to two double bonds and the 6- and 7-membered rings have zero to three double bonds, the heterocycle being optionally substituted with alkyl, halogen, hydroxy or alkoxy substituents,

further wherein the heterocyclyl optionally comprises a group chosen from:

- (i) bicyclic, tricyclic and tetracyclic groups in which any of the above heterocyclic rings is fused to one or two rings independently selected from an aryl ring, a cyclohexane ring, a cyclohexane ring, a cyclohexene ring, a cyclopentane ring, a cyclopentene ring, and another monocyclic heterocyclic ring;
- (ii) bridged bicyclic groups where a monocyclic heterocyclic group is bridged by an alkylene group optionally selected from

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$$\frac{H}{N}$$
, $\frac{1}{N}$, and

(iii) compounds of the formula

where X* and Z* are

independently selected from -CH₂-, -CH₂NH-, -CH₂O-, -NH- and -O-, with the proviso that at least one of X* and Z* is not -CH₂-, and Y* is selected from -C(O)- and -(C(R")₂)_v -, where R" is hydrogen or alkyl of one to four carbons, and v is 1-3.

2. (Twice Amended) A compound according to claim 1 wherein R³ is the group of formula II

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wherein R¹⁰, R¹¹, D, B, Y, Z, and n are defined as in claim 1; and R¹ is defined as in claim 1 with the proviso that if R³ does not define a pyrimidine, then R¹ is a pyrimidine.

3. (Twice Amended) A compound according to claim 1 of formula III

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$$(R^{12})_{p} \xrightarrow{\text{II}} S$$

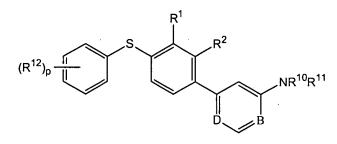
$$R^{5} \xrightarrow{\text{R}^{4}} D$$

$$(Z)_{n}^{p} BH$$

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wherein R¹, R², R⁴, R⁵, R¹⁰, R¹¹, R¹², D, B, Y, Z, and n are defined as in claim 1; and p is an integer of zero to five.

5. (Twice Amended) A compound according to claim 1 of formula IV



IV

wherein D and B are each independently selected from the group consisting of -N= and $-CR^6=$;

R¹ is selected from the group consisting of hydrogen, halogen and haloalkyl, with the proviso that if R³ does not define a pyrimidine, then R¹ is a pyrimidine; R² is selected from the group consisting of hydrogen, halogen and haloalkyl; R¹⁰ and R¹¹ are defined as in claim 1;

R¹², at each occurrence, is independently selected from the group consisting of halogen, alkyl, haloalkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl, wherein R¹² is unsubstituted or substituted with at least one electron donating group or electron withdrawing group; and

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p is an integer of zero to five.

7. (Twice Amended) A compound according to claim 1, selected from the group consisting of 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4yl)-piperidine-3-carboxylic acid, 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethylphenyl)-6-(3-(2H-tetrazol-5-yl)-piperidin-1-yl)-pyrimidine, 4-(4-(2-isopropylphenylsulfanyl)-3-trifluoromethyl-phenyl)-6-(4-(2H-tetrazol-5-yl)-piperidin-1-yl)pyrimidine, (1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4yl)-piperidin-3-yl)-methanol, 2-(1-(6-(4-(2-isopropylphenylsulfanyl)-3-trifluoromethylphenyl)-pyrimidin-4-yl)-piperidin-4-yl)-ethanol, 4-(6-(4-(2-isopropyl-phenylsulfanyl)-3trifluoromethyl-phenyl)-pyrimidin-4-yl)-morpholine, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidin-4-ol, 4-(6-(4-(2-isopropylphenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-2,5-dimethyl-morpholine, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3carboxylic acid amide, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)pyrimidin-4-yl)-piperidine-4-carboxylic acid amide, N-Ethyl-N-1-(6-(4-(2-isopropylphenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-pyrrolidin-3-yl)-acetamide, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3carboxylic acid ethyl ester, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethylphenyl)-pyrimidin-4-yl)-piperidine-4-carboxylic acid ethyl ester, 4-(6-(4-(2-isopropylphenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperazine-1-carboxylic acid ethyl ester, 4-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)piperazin-1-yl-acetic acid ethyl ester, (3-imidazol-1-yl-propyl)-(6-(4-(2-isopropylphenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-amine, 1-(6-(4-(2-isopropyl-

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phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-4-carboxylic acid, 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid diethyl amide, N-1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-pyrrolidin-3-yl)-acetamide, 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-6-(2-methoxymethyl-pyrrolidin-1-yl)-pyrimidine, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-pyrrolidin-3-ol, (1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-pyrrolidin-3-yl)-carbamic acid *tert*-butyl ester, isopropyl-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-methyl amine, and ethyl-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-methyl-amine.

12. (Amended) A compound according to claim 1 wherein A is an unsubstituted or substituted aryl group of the formula

wherein R¹² is defined as in claim 1; and p is an integer of 0 to 5.

14. (Amended) A compound according to claim 1 wherein R³ is selected from the group consisting of

 R^1 is defined as in claim 1 with the proviso that if R^3 does not define a pyrimidine, then R^1 is a pyrimidine.

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17. (Amended) A compound according to claim 1 wherein

R¹ is selected from the group consisting of hydrogen, halogen, alkyl and nitro, with the proviso that if R³ does not define a pyrimidine, then R¹ is a pyrimidine;

R² is selected from the group consisting of hydrogen, halogen, alkyl, and nitro;
R⁴ and R⁵ are each independently selected from the group consisting of hydrogen and alkyl; and

R³ is

wherein

D is $-CR^6 = \text{ or } -N =$,

B is -S -, -O -, $-CR^6 = \text{ or } -N =$,

Y is $-CR^6 = \text{ or } -N =$,

Z is $-CR^6 = \text{ or } -N =$; and

n is zero or one

18. (Amended) A compound according to claim 1 wherein

R¹ and R² are each independently selected from the group consisting of hydrogen, halogen, and haloalkyl;

R³ is a pyrimidine; and

R⁴ and R⁵ are each independently hydrogen.

19. (Amended) A compound according to claim 1 wherein

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R¹ is selected from the group consisting of hydrogen, halogen and haloalkyl, with the proviso that if R³ does not define a pyrimidine, then R¹ is a pyrimidine; R² is selected from the group consisting of hydrogen, halogen, and haloalkyl; R⁴ and R⁵ are each independently hydrogen; and

R³ is

wherein

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D is $-CR^6$ = or -N =,

B is -S-, -O-, -CR⁶= or -N=,

Y is $-CR^6$ = or -N =,

Z is -CR⁶= or -N=; and

n is zero or one.

20. (Amended) A compound according to claim 1 wherein

R¹ is selected from the group consisting of hydrogen, halogen and haloalkyl, with the proviso that if R³ does not define a pyrimidine, then R¹ is a pyrimidine; R² is selected from the group consisting of hydrogen, chloro, and trifluoromethyl;

R⁴ and R⁵ are each independently hydrogen; and

R³ is selected from the group consisting of

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